

Pharmacoinformatics for Drug Discovery

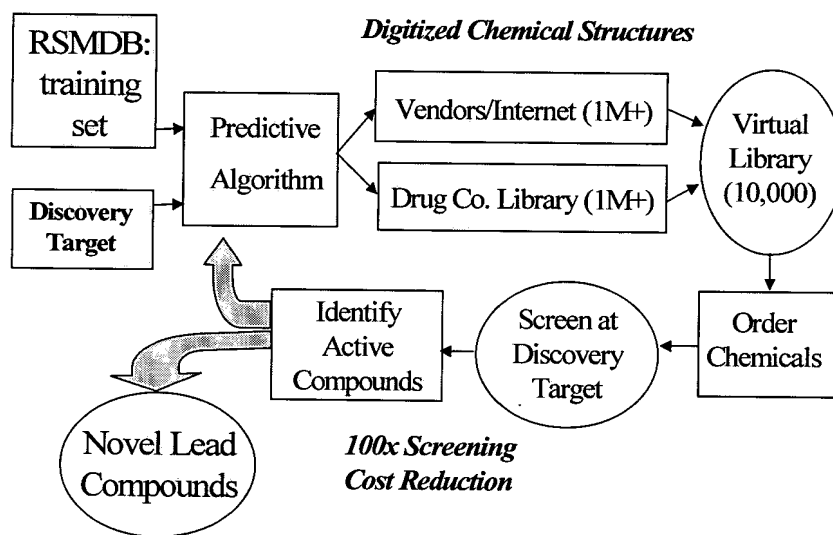


FIG. 1

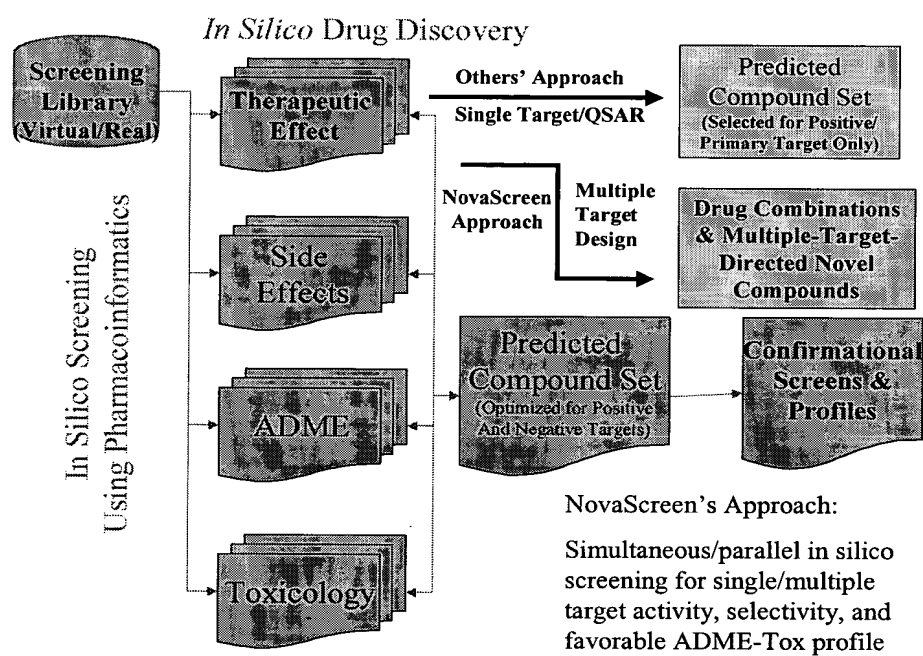


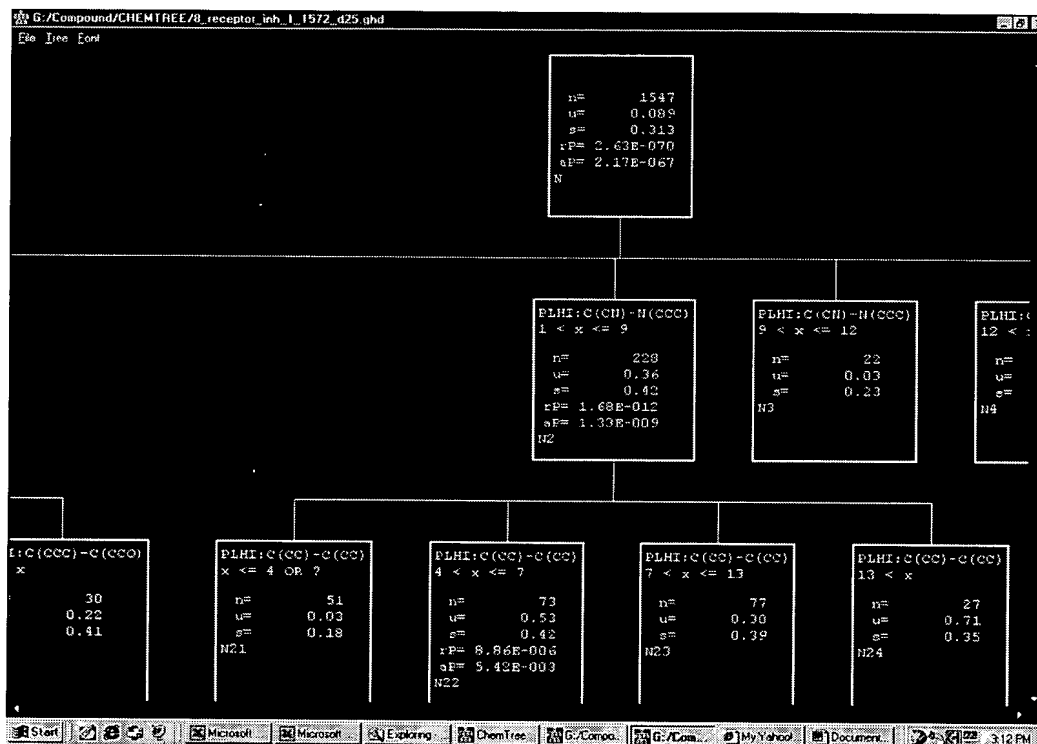
FIG. 2

$$\sum P_T = \sum P_D + \sum P_{UD}$$

$$\sum P_D = \sum P_{\text{prot}_1}^+ \sum P_{\text{prot}_2}^+ \sum P_{\text{prot}_n}^+ \cdots + \sum P_{\text{phys}_1}^+ \sum P_{\text{phys}_2}^+ \sum P_{\text{phys}_n} \cdots$$

$$\sum P_{UD} = \sum P_{\text{prot}_1_u}^+ \sum P_{\text{prot}_2_u}^+ \sum P_{\text{prot}_n_u}^+ \cdots + \sum P_{\text{phys}_1_u}^+ \sum P_{\text{phys}_2_u}^+ \sum P_{\text{phys}_n_u} \cdots$$

FIG. 3



500

FIG. 5

- PLHI: N(CC) - N(CC) X = 3
- PLLO: C(CCC) - N(CC) X = 2
- PLHI: C(CCC) - N(CC) X = 5
- PLLO: C(CNN) - N(CC) X = 1
- PLHI: C(CNN) - N(CC) X = 2

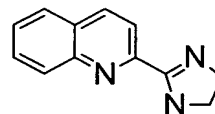


FIG. 6

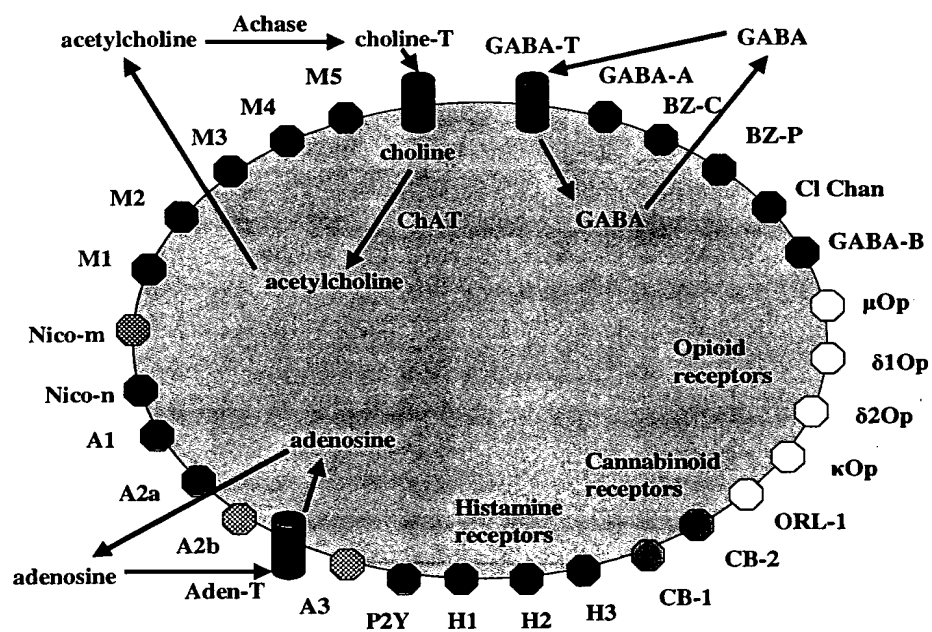


FIG. 7

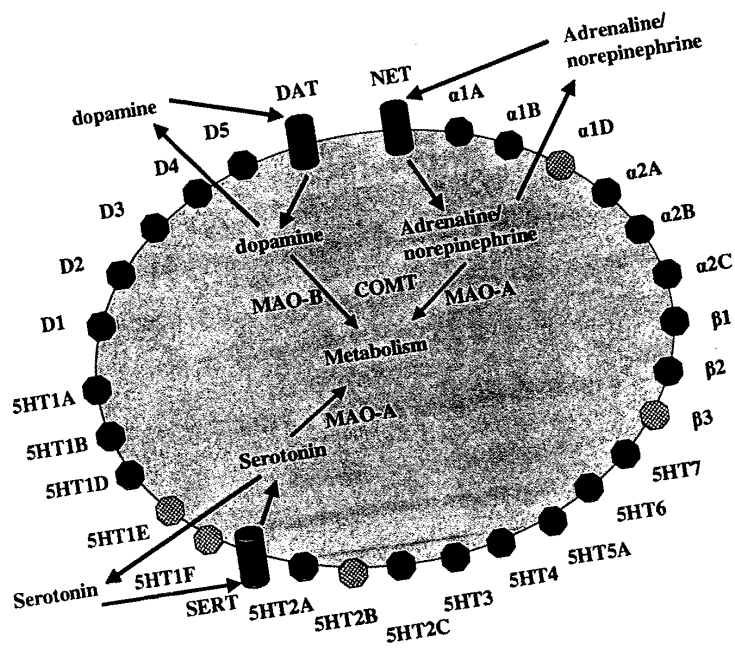


FIG. 8

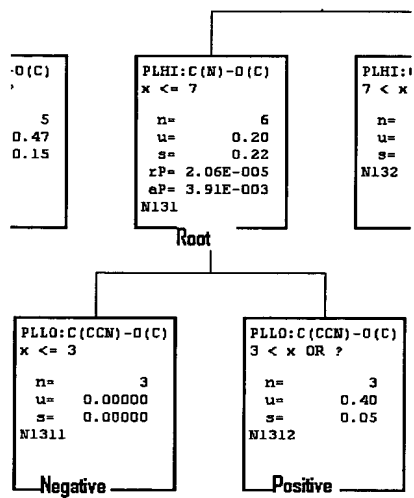


FIG. 9

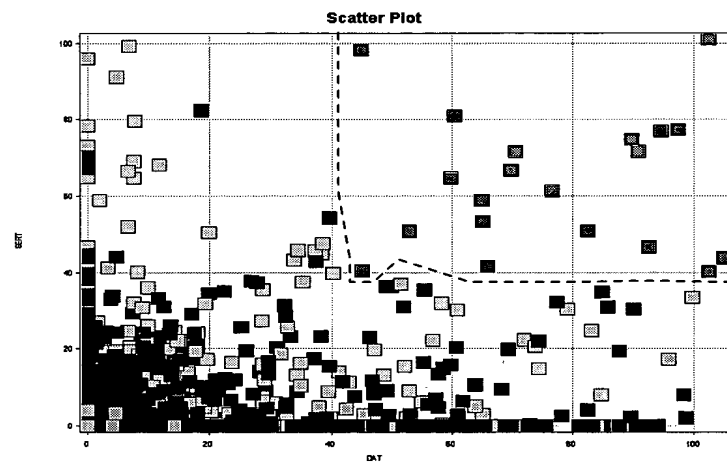


FIG. 10

PHARMACoinFORMATICS

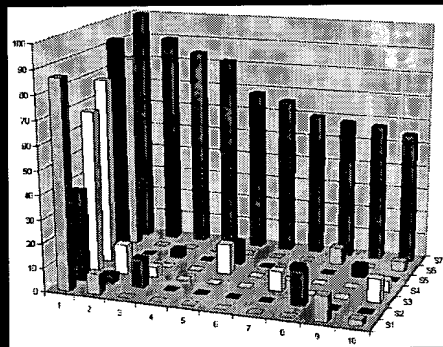
Single Step Approach to Optimized Leads

An Example of Finding Better and Cleaner Drug Candidates

in silico screen 240,000 cmpds

- 400 Compounds
- 34 Hits
- 5 Structural Classes
- 9 Hits with Desired Target Specificity

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FIG. 11

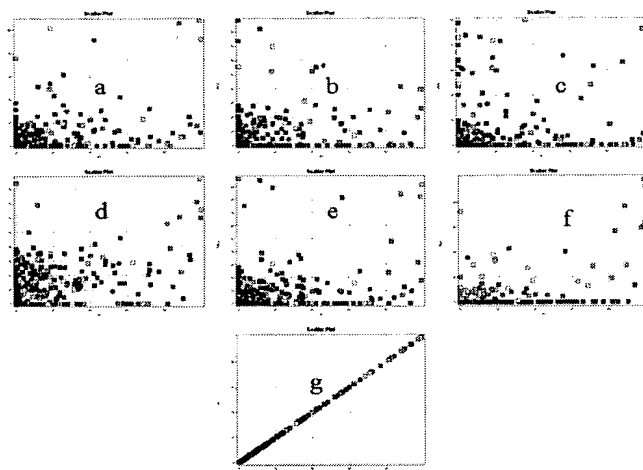


FIG. 12

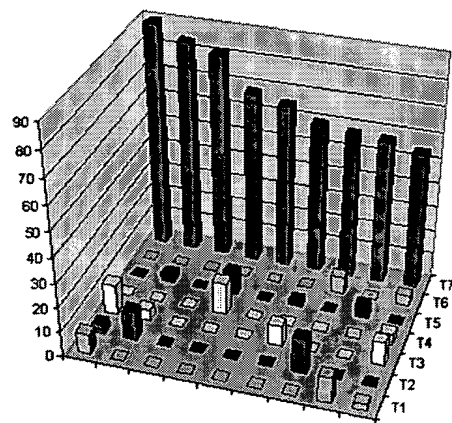


FIG. 13

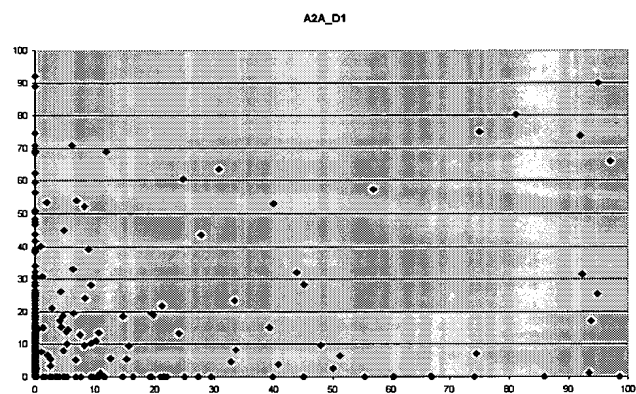


FIG. 14

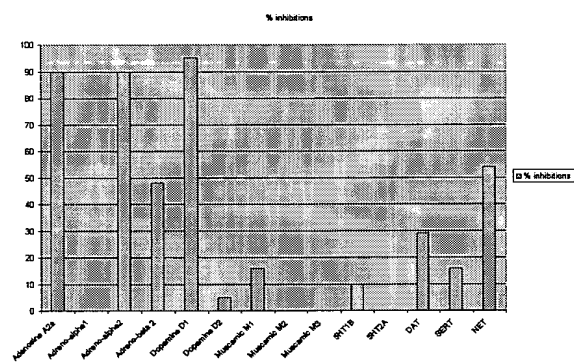


FIG. 15

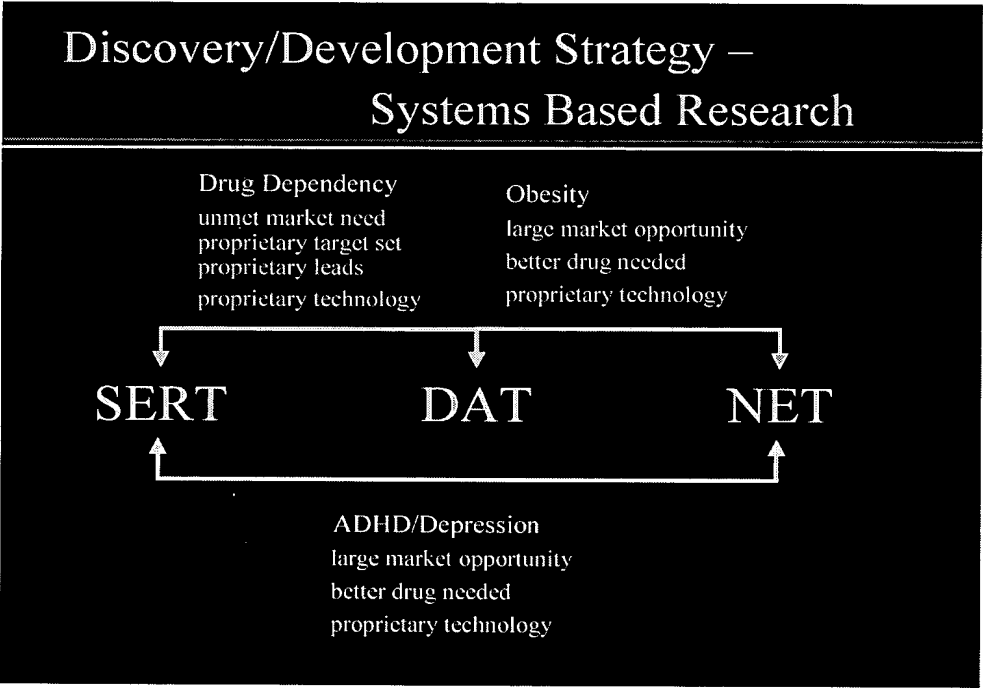


FIG. 16

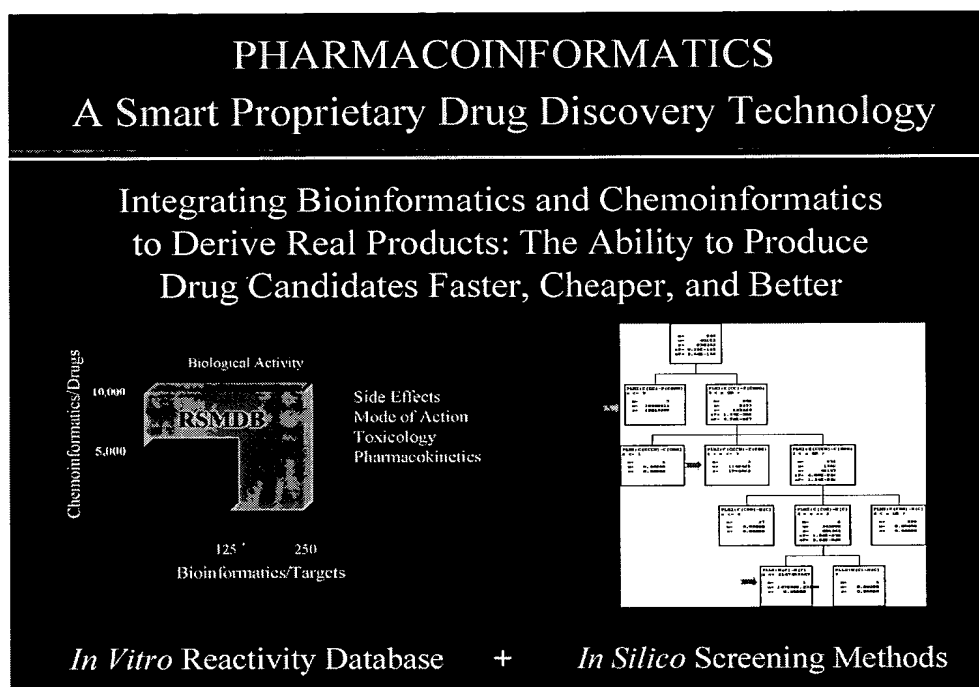


FIG. 17

RSMDB Content: Compound Classes

- Prescription Drugs (1500-2000)
- OTC Medicines; Veterinary Medicines
- Agricultural/Environmental Chemicals
- Drugs in Clinical Trials (& like structures)
- Discontinued/Failed Drug Candidates
(and like/similarity structures)
- Pharmacological Reference Agents
- Bioactive Natural Products
- + Structurally Diverse Chemical Compounds

FIG. 18

RSMDB Content: Target Classes

- Drug Discovery Molecular Targets
 - Receptors Enzymes
 - Transporters Ion Channels
 - Enriched set of market-validated GPCR targets, especially for CNS diseases
- Side Effect Targets
- *In Vitro* Toxicology Targets
- *In Vitro* Pharmacokinetic Targets
- Selected from 300 Available Developed Assays

FIG. 19

Pharmacoinformatics: Compressing the Drug Discovery and Development Timeline

Drug Industry Standard: 10-12 Years to Market

The diagram illustrates the drug discovery and development timeline. A horizontal timeline starts at '10 Yrs' and ends at '0'. The timeline is divided into stages: Target, Library Screen, Optimize, Preclinical, Clinical, and NDA. A solid arrow represents the standard timeline, while a dashed arrow represents the compressed timeline using RSMDb and *in silico* screening. The compressed timeline is labeled 'RSMDb and *in silico* screening: one-step optimization' and 'New uses of known safe compounds; RSMDb focus on validated drug targets'.

10 Yrs 5 Yrs 0

Target Library Screen Optimize Preclinical Clinical NDA

RSMDb and *in silico* screening: one-step optimization

New uses of known safe compounds;
RSMDb focus on validated drug targets

FIG. 20

PHARMACONFORMATICS

New Economics of Drug Discovery

Cost comparison of discovery economics

240,000 compounds $\xrightarrow{\text{in silico}}$ 400 compounds $\xrightarrow{\text{in vitro}}$ 34 hits

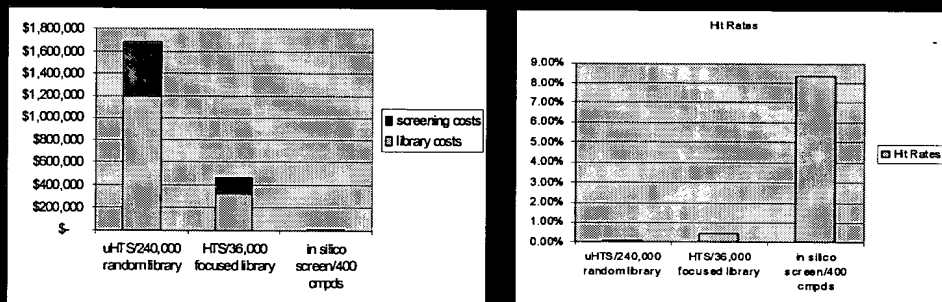


FIG. 21